REMARKS

Claims 22-24 are now in the application, and are directed to the elected invention. Claim 22 has been amended for purposes of clarity to more clearly point out the elected invention. Also Claim 22 has been amended to recite "or a functional derivative thereof" to provide the needed antecedent basis for the term present in Claim 23.

Claim 23 has been amended to correct the spelling of "growth".

The rejection of Claims 22-24, 28 and 30 under 35 U.S.C. 112, ¶1 has been overcome by the amendment to the claims. In particular, the claims now explicitly recite "increasing insulin sensitivity."

Also, the rejection of Claim 20 (presumably also Claim 23) under 35 U.S.C. 112¶2 for lack of antecedent basis has been overcome by the amendment to generic Claim 22.

The rejection of Claims 19-21 under 35 U.S.C. 102(b) over Sönksen et al. is no longer applicable since Claims 19-21 have been cancelled.

Claims 19-24 and 27-30 were rejected under 35 U.S.C. 103(a) as being unpatentable over Sönksen et al. Sönksen et al. does not render obvious the present invention. In particular, the present claims clarify that the method relates to treating patients having the Metabolic Syndrome and are non-insulin dependent patients. In another words these patients are at risk of acquiring type 2 diabetes or already have type 2 diabetes, and are insulin resistant. This is a very specific group of patients.

Insulin resistance is believed to have a major pathogenic role in the development of type 2 diabetes mellitus (previously named non-insulin dependent diabetes mellitus; NIDDM) and for the induction of hypertension and other metabolic consequences of the Metabolic Syndrome

(also named Syndrome X). (See Reaven GM, Lithell H, Landsberg L. Hypertension and Associated Metabolic Abnormalities-The Role Of Insulin Resistance and the Sympathoadrenal System. N Engl J. Med 1966; 334:374-381) whereas, increased insulin sensitivity i.e. the reverse is not known to be primarily involved in any metabolic disease.

Type 2 diabetes is therefore treated with all possible interventions that can increase the insulin sensitivity. When these treatment modalities fail, insulin is introduced in order to control glucose levels. This does not convert type 2 into type 1 diabetes (formerly IDDM) as the primary pathophysiological condition remains i.e. the insulin resistance.

By the use of GH, the insulin sensitivity is increased and therefore GH can be used both for preventing and treating NIDDM.

Sönksen, U.S. Patent No. 5,426,096 does not render obvious the present invention since, among other things, Sönksen bases the findings therein on the known GH insulin-antogonistic (diabetogenic) effect. Sönksen used this effect for inhibition of hypoglycemia for patients having diabetes who are on insulin treatment (IDDM), but he does not treat the diabetes disease itself. By giving GH according to Sönksen, the insulin sensitivity is reduced and by that it may have poor influence on other metabolic conditions associated with diabetes as mentioned above.

Sönksen therefore prevents only the adverse effects of the treatment with insulin, which is used for treatment of diabetes (IDDM and NIDDM).

The present claims relate to the reverse action of GH, which is a new and unexpected finding. By giving the group of non-insulin dependent patients (NIDDM, type 2 diabetes mellitus) GH for a certain period of time, the patients become more sensitive to insulin, their

insulin sensitivity is increased and thereby their risk of developing type 2 diabetes mellitus in the future can be reduced.

In the office action, the Examiner states: "An ordinary art skilled . . . would have reasonably expected to successfully treat a patient having diabetes (IDDM or NIDDM) with GH. However the success rate would have been expected to be greater for NIDDM patients as with IDDM patient - in view of the reference's teachings."

This is not true. It has been found pursuant to the present invention, that IDDM patients and NIDDM patients react differently on GH. A decreased insulin sensitivity gives a risk for development of NIDDM and is an important pathophysiological mechanism for those patients who already are NIDDM. The group to be treated according to the present invention are individuals with an insulin resistance who are at risk for cardiovascular diseases and development of NIDDM, while healthy persons with a normal insulin sensitivity probably will not change the insulin resistance when GH is administered.

GH has until now been regarded as a diabetogenic hormone which increases the insulin resistance and by that induces the metabolic consequences of this with increased blood glucose, high levels of total cholesterol and triglycerides and low levels of high-density lipoprotein (HDL) cholesterol. Type 2 diabetes can be treated with insulin, but despite this it is not a type 1 diabetes or IDDM.

The findings of the present invention must be regarded as surprising and unexpected over Sönksen and could not have been expected from Sönksen.

It has unexpectedly been found that GH treatment can improve insulin resistance for a specific group of patents. Insulin resistance must exist for the development of NIDDM. By

improving the insulin resistance by treatment with GH, this type of diabetes can be inhibited for the treated group of this invention.

Concerning the rejection under 35 U.S.C. 103, one must keep in mind that the properties of the subject matter and improvements which are inherent in the claimed subject matter and disclosed in the specification are to be considered when evaluating the question of obviousness under 35 U.S.C. 103. *See Gillette Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ2d 1923 (Fed. Cir. 1990), *In re Antonie*, 195 USPQ 6 (CCPA 1977), *In re Estes*, 164 USPQ 519 (CCPA 1970), and *In re Papesch*, 137 USPQ 43 (CCPA 1963).

No property can be ignored in determining patentability and comparing the claimed invention to the prior art. Along these lines, *see In re Papesch*, supra *In re Burt et al.*, 148 USPQ 548 (CCPA 1966), *In re Ward*, 141 USPQ 227 (CCPA 1964), and *In re Cescon*, 177 USPQ 264 (CCPA 1973).

In view of the above, consideration and allowance are, therefore, respectfully solicited.

In the event that the Examiner believes an interview might serve to advance the prosecution of this application in any way, the undersigned attorney is available at the telephone number noted below.

The Commissioner is hereby authorized to charge any fees or credit any overpayment associated with this communication including any extension fees to Deposit Account No. 22-0185.

Respectfully submitted,

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